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**13. ABSTRACT** *(Maximum 200 Words)*

This renewal report is for an academic award for Prof. Leroy Chapman to pursue a program of study to apply Diffraction Enhanced X-ray Imaging applied to mammography and other areas of medical imaging.
Prof. Chapman is a co-developer of the technique and intends to determine the applicability of that technique to the imaging of cancerous tissue possibly allowing earlier or more reliable detection. Being a new researcher in breast cancer imaging, he intends to become more proficient in mammography and look for opportunities to apply the Diffraction Enhanced Imaging technique to other areas of medical imaging.
This award has allowed Prof. Chapman to:

1) explore the potential application of Diffraction Enhanced Imaging to mammography,
2) understand at a fundamental level the DEI process and the sources of contrast,
3) become more aware of the current state-of-the-art in mammography, breast cancer research, and medical imaging,
4) explore the possibility of developing a dedicated imaging program at the Advanced Photon Source, with the major imaging research program being the application of DEI to medical imaging, and
5) pursue the development a laboratory / clinical based DEI imaging system.

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May 27, 2001

PI - Signature Date

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## Introduction

Prof. Chapman has been involved for the last several years with medical imaging projects associated with synchrotron radiation [1-9]. More recently, he was a co-developer of the Diffraction Enhanced Imaging (DEI) technique [1-4,9]. With a background in x-ray optics, synchrotron radiation, and solid-state physics, his present research is solely directed to medical imaging projects. He became initially involved with the transvenous coronary angiography project as physicist working on the monochromator associated with that program at the National Synchrotron Light Source [5]. Since then, he has become more involved with the medical imaging research performed with that and other programs, including the synchrotron mammography program to explore the use of monoenergetic x-rays. This program was Prof. Chapman's first experience in mammography. Given his many years in synchrotron radiation and construction and operation of beamlines, he was also appointed director of IIT's Center for Synchrotron Radiation Research and Instrumentation (CSRRI). *As a direct result of receiving this academic award(in year 1 of this award), he has given up the directorship of the CSRRI to focus entirely on research and exploring applications of x-ray optics to medical imaging problems.* The purpose of his research is to evaluate DEI and other diffractive optics applied to imaging for its application to mammography and other areas of medical imaging. He intends to pursue this research and in order to be successful in applying this and other diffraction techniques to this area, he is becoming more proficient in this the area of medical imaging research.

**Objectives**

1. Explore the potential application of Diffraction Enhanced Imaging to mammography.
2. Understand at a fundamental level the physics of the DEI process
3. Become proficient in the language and current state-of-the-art in mammography, breast cancer research, and medical imaging.
4. Develop a dedicated imaging program at the Advanced Photon Source, with one of the major imaging research programs, being the application of DEI to mammography and to medical imaging.
5. Develop a conceptual design of a conventional x-ray source DEI system for mammography.

## Body

The approved statement of work in the original proposal addresses the objectives of Prof. Chapman. In the text that follows the statement of work item is italicized and the accomplishments associated with that item follows.

**Statement of work**

***Application of Diffraction Enhanced Imaging to Medical Imaging***

***Task 1.*** *Understand the DEI technique.*

- *Study image quality of mammography phantoms obtained with the DEI technique (both qualitative and quantitative studies).*

- *develop phantoms which will allow quantification (MTF and sensitivity) of absorption, refraction and extinction (year 1-3).*

The test objects that assess and quantify refraction and absorption have been constructed and evaluated. At this point in the proposed program, a modulation transfer function (MTF) test object has not been developed.

The major accomplishment in this area is a new method of DE imaging that allows the complete independent determination of objects refraction, absorption, extinction and the scatter distribution width. This technique requires that several images be taken through the rocking curve. Although this appears to require more dose for the multiple images, it may in fact require less. Based on the methods used in computed tomography, the images may be taken at low dose. These various images will then be fit to model functions that assess the objects "generalized scattering function". This scattering function has the following information content: the centroid of the function contains the refraction angle information (similar to DEI, but not affected by the

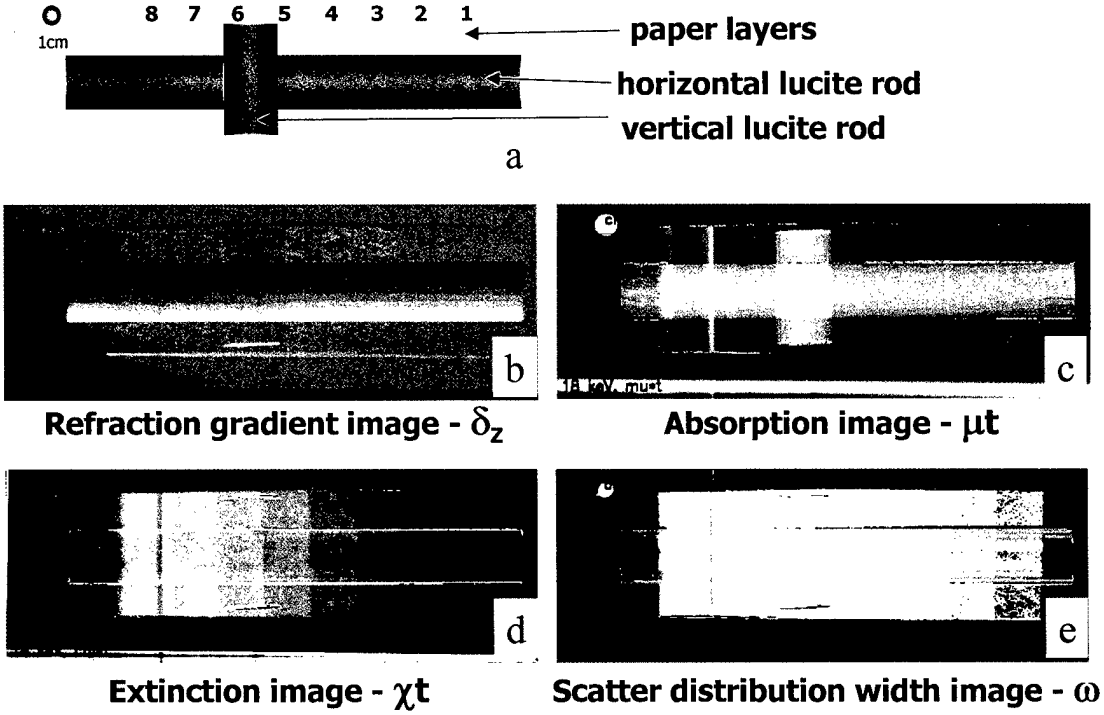


Figure 0 Preliminary analysis of the refraction, absorption and extinction test object shown in a. The lucite rods give refraction and absorption contrast. The paper layers give the scattering or extinction effect. Date was acquired at the NSLS in July 2000 at 18keV using a Si(3,3,3) monochromator and analyzer system. 24 images acquired from –10.8mr to +9.9 mr in 0.9 mr steps. Each pixel in the images were analyzer using a physical model to arrive at the refraction gradient image (b), absorption image (c), extinction image (or scatter rejection image) (d), and the scatter distribution width image (e).

simultaneous extinction), the absorption from the integral of the function, the extinction from the absorption corrected amplitude of the peak, and the ultra-small angle scattering width from the width of the distribution. The extinction and scattering width represent new images to radiography and the refraction image is unaffected by the extinction

occurring in the object. At this point, I feel this will be the way that DEI will be performed in the future. An example of this new method is shown for a test object (figure 1) and excised tissue sample (figure 2).

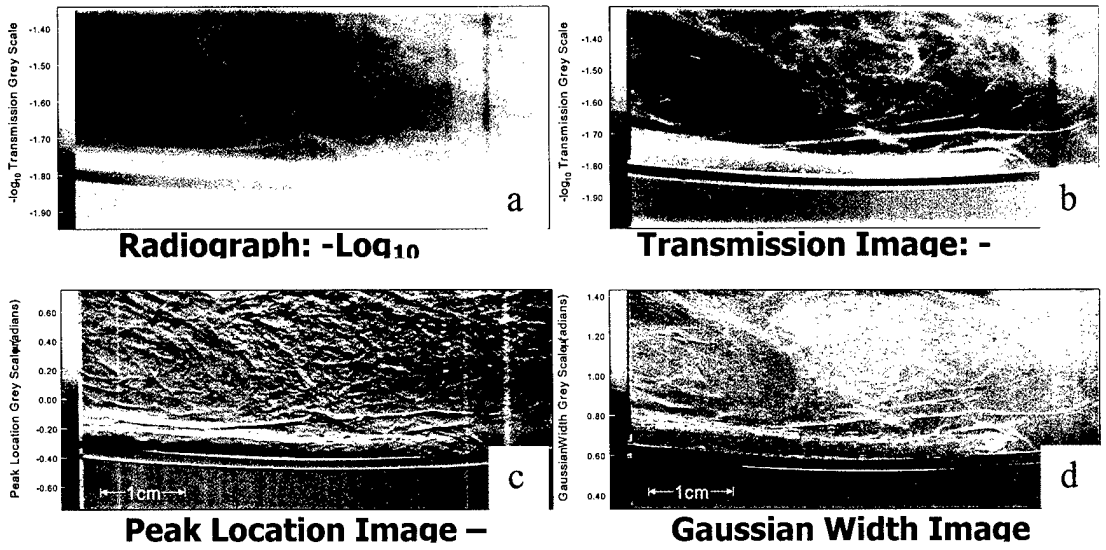


Figure 2 Preliminary analysis of cancerous excised breast tissue acquired at the NSLS in January 2001 at 18keV using a Si(3,3,3) monochromator and analyzer system. 18 images acquired from -8.1mr to +7.2 mr in 0.9 mr steps. Each pixel in the images were analyzer using a gaussian model to arrive at the radiograph (a), transmission image; similar to extinction image(b), peak location or refraction gradient image©, and gaussian width image(d).

- *image these phantoms and compare against conventional radiography and non-analyzer synchrotron imaging (year 1-3).*

Test objects have been created and imaged to assess the refraction sensitivity and extinction sensitivity of DEI. Again see figure 1. Figure 1 shows a combined refraction, absorption, and extinction test object to assess the DEI sensitivity to detect and to successfully extract refraction gradient, extinction and absorption information.

- *evaluate imaging geometries, Bragg (reflection) or Laue (transmission) analyzer geometry.*

The Bragg and Laue analyzer geometries have been evaluated for the task of imaging excised human tissue samples with cancer as was previously reported.

- *evaluate the optimal imaging energy for sources of contrast.*

Images at several energies (18, 20, 25, 30 keV) have been taken of test objects and tissues containing cancer. These images are presently being assess by Dr. Etta Pisano as part of an observer study.

***Task 2.*** *Apply the DEI technique.*

- *Study human and animal tissue samples to determine if contrast exists for tumor tissue using the DEI technique.*
  - *obtain animal and human tissue samples possibly with intact tumor tissue (year 1)*

As discussed in the previous tasks, tissue samples with cancer have been obtained (from UNC) and imaged under a variety of conditions.

- *image these samples and optimize imaging conditions to enhance tumor contrast (year 1-3)*

As reported previously the tissue samples are being imaged at a variety of imaging conditions. Bragg and Laue geometries, using a variety of reflections (Si (1,1,1), Si ( 3,3,3), Si(5,5,5) ), using various imaging energies ( 18, 25, and 30keV), and at various points in the rocking curve ( top, +/- ½ Darwin width, +/- 1 Darwin width) and a radiograph for comparison.

- *develop techniques for 'reading' images (year 1-3)*

The radiographer collaborator in the project, Etta Pisano, MD, has assessed the images and has written a paper that discusses some the features which are seen in the images using DEI and correlated these features with pathology. This work is summarized in a recent publication in Radiology [9].

- *image phantom and tissue samples with both Bragg and Laue geometries and assess which system affords the best contrast for refraction and/or extinction (year 2)*

This work has been completed.

***Task 3.*** *Growth as a breast cancer researcher*

- *attend seminars and workshops on mammography, breast cancer research, and medical imaging research (year 1-3)*

I have attended several workshops and symposia including:

- "Medical Applications of Diffraction Enhanced Imaging", European Synchrotron Radiation Facility, 12 October 2000, Grenoble, France.
- "Medical Applications of Diffraction Enhanced Imaging", Biomedical Engineering in the 21st Century Symposium, 29 March 2001, IIT.
- "The Compact Source Problem", Medical Research Conference, European Synchrotron Radiation Facility, 1-3 March 2001
- "Medical and Biological Applications of Diffraction Enhanced Imaging", Biomedical Engineering Seminar Series, Argonne National Laboratory, University of Chicago, and Illinois Institute of Techonology, 13 February 2001, Argonne National Laboratory
- "Application of Diffraction Enhanced Imaging to Osteoarthritis Research", with Carol Muehleman (Rush University), Research Rounds Seminar Series, Rush St. Lukes Presbyterian Medical Center and Rush University, 11 April 2001.

- *strengthen liaisons with Rush Memorial Hospital and develop collaboration with other Chicago area breast cancer researchers (year 1)*

I have established a collaboration with Rush University in both bone and osteoarthritis research and have spoken at that university about DEI and synchrotron based imaging.

***Task 4.*** *Develop imaging research facility at the Advanced Photon Source*

- *identify core group users for both medical and materials imaging (year 1)*

I have established collaborations with researchers from IIT, Rush University, University of Chicago, Henry Ford Hospital (Detroit), University of North Carolina, North Carolina State University, and Brookhaven National Laboratory. All of the collaborations are using DEI for a variety of applications in mammography, osteoarthritis and bone research.

- *define the experimental programs (year 1)*

The experimental programs are in the areas of x-ray optics for imaging, DEI, mammography, osteoarthritis, and bone imaging.

- *prepare Conceptual Design Report and proposals for funding the program (year 2-3)*

A proposal to the NIH Biomedical Research Partnerships (BRP) has been prepared and submitted – pending review.

***Task 5.*** *Technology transfer to conventional imaging systems*

- *Determine parameters necessary to successfully apply DEI to mammography (year 1-3)*
  - *Explore x-ray optics options for conventional x-ray sources (year 1-3)*

I have done extensive research into a variety of novel x-ray source and optics that

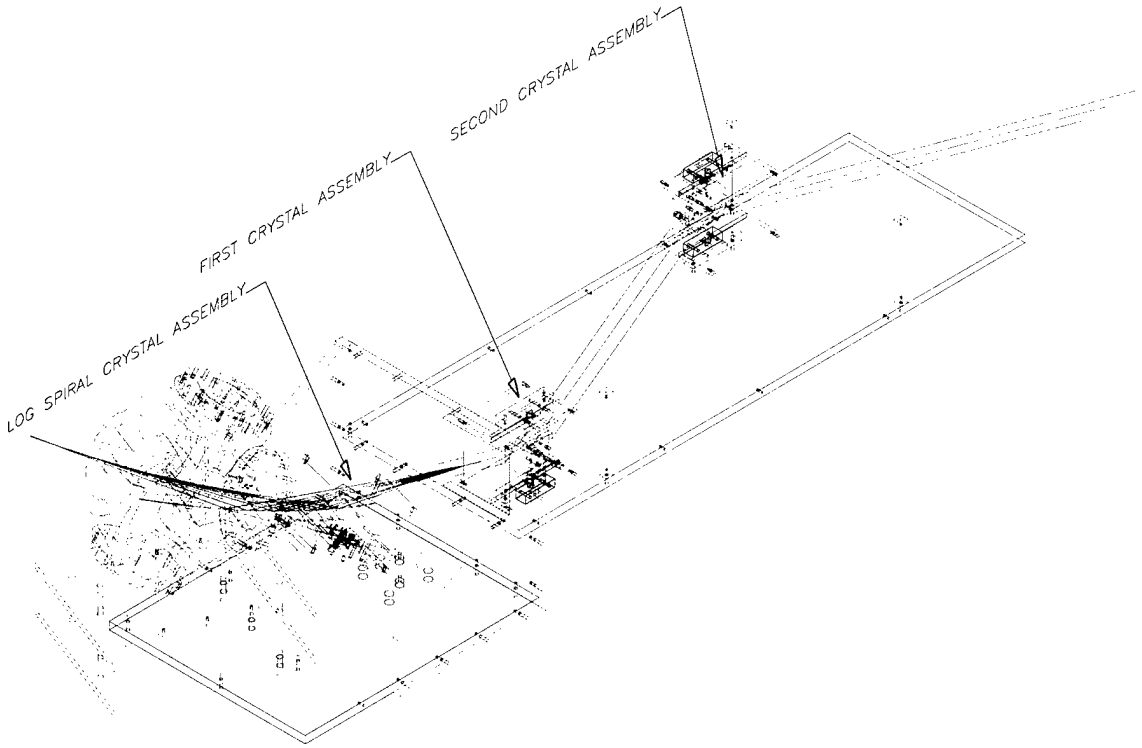


Figure 3 Design of DEI system for prototyping source and crystal concepts. Shown is the x-ray source, spiral bent crystal pre-monochromator, first crystal assembly (DEI monochromator) and second crystal assembly (analyzer). The system will allow an extended source and will be capable of producing DE images without scanning the object and detector.

might allow a conventional x-ray tube based system to be developed for DEI. A

conceptual design that will allow testing of these source and crystal systems has been completed (see next bullet).

- *Develop conceptual design for conventional x-ray source system (year 3)*

The conceptual design of a second-generation DEI system is completed and construction is nearing completion. This system will allow novel x-ray source and crystal geometries to be tested easily. A cut-away view of this system is shown in figure 3.

- *If feasible, seek funding / industrial partners for a clinical based DEI system (year 3)*

Glaxo-Wellcome is very interested in DE imaging for osteoarthritis and other applications. Glaxo-Wellcome is paying patent application fees (US and International) for "Diffraction Enhanced X-ray Imaging of Articular Cartilage". We are in the process of exploring the possibility of developing an industrial collaboration (c.f. Industrial Macromolecular Crystallography Association – IMCA) that may pool resources to perform animal and tissue imaging studies at a imaging facility at the Advanced Photon Source.

## Key Research Accomplishments

- Developed new method to apply a multiple image analysis to expand the information extraction from DE imaging – refraction gradient, absorption, extinction, and scatter distribution width. These may prove useful for breast tissue imaging and may ultimately result in dose reduction using "CT like" statistical algorithms.
- Developed a test bed for x-ray source and x-ray optics for the laboratory (and possibly clinical) application of DEI using non-synchrotron based sources.
- Developed test objects for the evaluation of refraction, absorption, and extinction.

## Reportable Outcomes

**Manuscripts**

- Pisano ED, Johnston RE, **Chapman D**, Geradts J, Iacocca MV, Livasy CA, Washburn DB, Sayers DE, Zhong Z, Kiss MZ, Thomlinson WC. Human Breast Cancer Specimens: Diffraction-enhanced Imaging with Histologic Corrlation - Improved Conspicuity of Lesion Detail Compared with Digital Radiography. Radiology 2000: 414(3); 895-901.
- C. Karanfil, **L.D. Chapman**, G.B. Bunker, C.U. Segre, and N.E. Leyarovska, A 'Beam Cleaner' for Harmonic Selection / Rejection, Proceedings of 11$^{th}$ National SRI Conference, AIP CP 521, 276-282 (2000).
- C. Karanfil, Z. Zhong, **L.D. Chapman**, R. Fischetti, G.B. Bunker, C.U. Segre, and B.A. Bunker, A Bent Laue Analyzer Detection System for Dilute Fluorescence XAFS, Proceedings of 11$^{th}$ National SRI Conference, AIP CP 521, 178-182 (2000).

- I.Ivanov, G. Rosenbaum, J. Chrzas, R. Fischetti, C. Segre, and **D. Chapman**, A robust cryogenic crystal design in use at the APS, Proceedings of 11th National SRI Conference, AIP CP 521, 271-275 (2000).
- C.U. Segre, N.E. Leyarovska, **L.D. Chapman**, W.M. Lavender, P. Plag, A.K. King, A.J. Kropf, B.A. Bunker, K. Kemner, P. Dutta, R.S. Duran and J. Kaduk, The MRCAT Insertion Device Beamline at the Advanced Photon Source, Proceedings of 11th National SRI Conference, AIP CP 521, 419-422 (2000).
- B. Ren, F. A. Dilmanian, **L.D. Chapman**, X. Y. Wu, Z. Zhong, I. Ivanov and X. Huang, "Interpretation of bent-crystal rocking curves using phase-space diagram". Nucl. Instrum. Meth. in Phys. Res. accepted for publication.
- Z. Zhong, W. Thomlinson, **D. Chapman** and D. Sayers, "Implementation of Diffraction Enhanced Imaging Experiments: at the NSLS and APS", Nucl. Instrum. Meth. in Phys. Res. A. accepted for publication, 2/1/2000.

**Presentations**

**Symposia Talks**

- "Medical Applications of Diffraction Enhanced Imaging", European Synchrotron Radiation Facility, 12 October 2000, Grenoble, France.
- "Medical Applications of Diffraction Enhanced Imaging", Biomedical Engineering in the 21st Century Symposium, 29 March 2001, IIT.

**Colloquia**

- Valparaiso University Physics Department Colloquium – Sept 29, 2000

"Physics and Applications of Diffraction Enhanced X-ray Imaging"

**Conferences**

- "The Compact Source Problem", Medical Research Conference, European Synchrotron Radiation Facility, 1-3 March 2001, (canceled as talk and given as poster due to root canal).

**Seminars**

- Argonne National Laboratory, University of Chicago, and Illinois Institute of Techonology Biomedical Engineering Seminar Series, "Medical and Biological Applications of Diffraction Enhanced Imaging", 13 February 2001, Argonne Guest House
- "Application of Diffraction Enhanced Imaging to Osteoarthritis Research", with Carol Muehleman (Rush University), Research Rounds Seminar Series, Rush St. Lukes Presbyterian Medical Center and Rush University, 11 April 2001.

E-MAPS Outreach Seminars to potential IIT students on IIT research activities:

- 26 October 2000 – forgot the name of the school
- 3 November 2000 – forgot name of school
- 30 November 2000 – forgot name of school
- 28 March 2001 – Queen of Peace Academy

**Patents and licenses applied for and/or issued**

- **L.D. Chapman**, et.al., " Diffraction Enhanced X-ray Imaging of Articular Cartilage", filed (IIT 160 provisional).
- **L.D. Chapman**, et.al., "X-ray Line or Point Source using a Shaped Source and Bent Crystal Optics", disclosure to IIT patent committee.

- M. Wernick, **L.D. Chapman**, et. al., "An imaging method based on ultra-small-angle scattering of x rays", disclosure to IIT patent committee.

**Funding applied for based on work supported by this award**

- PI – Diffraction Enhanced Imaging applied to Mammography, National Institutes of Health R21, $173K, funded in second year.
- Co-PI with Klaus Kuettner, PI, Rush University, Novel X-ray Techniques for Osteoarthritis Research, submitted to National Institutes of Health Biomedical Research Partnerships. Approximate budget 2.5M$ over 5 years. Submitted February 2001 (pending review)
- Co-PI with Etta Pisano, PI, University of North Carolina, Development of a Compact Diffraction Enhanced Imaging System Prototype submitted to National Institutes of Health Biomedical Research Partnerships. Approximate budget 7M$ over 5 years. IIT subcontract approximately 2.5M$. Submitted November 2000 (didn't get fundable score)
- PI - X-ray Optics for Diffraction Enhanced Imaging, NIH/NCI R21 Proposal, February 2001, ~400K$/2years (pending review).
- Co-Investigator - Medical Imaging at the NSLS, (Zhong, PI), subcontract to cover travel expenses research, ~5K$/year (pending review).
- Co-Investigator (David Baker-PI) - part of DARPA proposal to develop high tech programs on Chicago's south side (~1.5M$/year for 3 years to develop clinical DEI system in "incubator") (pending review).

## *Conclusions*

The academic award has allowed Prof. Chapman to focus on DEI and x-ray optics research directed to mammography and medical imaging. This has led to the development of new techniques for the application of DEI to conventional sources and the discovery of a new method of image acquisition and analysis that may lead to lower dose and increased information extraction. In addition, the extension of the technique to other areas of radiography has continued; DEI continues to show promise for the detection of damage in joints (both animal and human tissues). This grant has allowed Prof. Chapman to become more proficient as a medical researcher in mammography and other areas of medical research. Also, Prof. Chapman continues to pursue the development of a dedicated medical imaging facility at the Advanced Photon Source at which applications of DEI will be explored as well as x-ray optics which may allow the application of DEI using conventional sources.

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## *Appendices*

None